

U.S. Patent Application No. 09/628,186
Amendment dated January 6, 2005
Responsive to the office action of August 6, 2004
Attorney Ref. No.: 037003-0280721
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I. AMENDMENT

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method for radiolabeling a chelator-conjugated ~~protein, ligand or peptide~~ antibody or antibody fragment with a therapeutic radioisotope for administration to a patient comprising
 - (i) mixing the chelator-conjugated ~~protein, ligand or peptide~~ antibody or antibody fragment with a solution comprising the therapeutic radioisotope or salt thereof, and
 - (ii) incubating the mixture for a sufficient amount of time under amiable conditions such that a radiolabeled ~~protein, ligand or peptide~~ antibody or antibody fragment is produced having sufficient radioincorporation ~~greater than 95%~~, sufficient binding specificity immunoreactivity, and a specific activity of at least about 5 mCi/mg, ~~is achieved~~ such that the radiolabeled ~~protein, ligand or peptide~~ antibody or antibody fragment may be administered directly to the patient without further purification of the radiolabeled antibody or antibody fragment from unincorporated radioisotope.
2. (Original) The method of claim 1, wherein said therapeutic radioisotope is selected from the group consisting of alpha and beta emitters.
3. (Original) The method of claim 2, wherein said therapeutic radioisotope is a beta emitter.
4. (Original) The method of claim 3, wherein said beta emitter is ⁹⁰Y.
5. (Currently amended) The method of claim 1, wherein ~~said protein or peptide is an antibody or antibody fragment~~ a level of radioincorporation of greater than 95 % is achieved.
6. (Original) The method of claim 4, wherein said sufficient incubation time is less than about eight minutes.

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7. (Original) The method of claim 6, wherein said sufficient incubation time is between about 30 seconds to about five minutes.

8. (Original) The method of claim 1, wherein said chelator is a bifunctional chelator selected from the group consisting of MX-DTPA, phenyl-DTPA, benzyl-DTPA, CHX-DTPA, DOTA and derivatives thereof.

9. (Original) The method of claim 8, wherein said chelator is MX-DTPA.

10. (Currently amended) The method of claim 4 1, wherein said amiable conditions refer to acceptable temperature, pH and buffer conditions.

11. (Original) The method of claim 10, wherein said acceptable temperature ranges from about 25°C to about 50°C.

12. (Original) The method of claim 10, wherein said acceptable pH ranges from about 3 to about 6.

13. (Original) The method of claim 10, wherein said acceptable buffer is an acetate buffer.

14. (Original) The method of claim 13, wherein said buffer is sodium acetate is at a concentration of between about 10 and about 1000 mM.

15. (Original) The method of claim 10, where said acceptable buffer includes a benign radioprotectant.

16. (Original) The method of claim 15, wherein said benign radioprotectant is ascorbate.

17. (Canceled)

18. (Currently amended) The method of claim 1, wherein said ~~binding specificity~~ immunoreactivity is at least 70%.

19-48. (Canceled)

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49. (Previously presented) The method of claim 6, wherein said sufficient incubation time is about three minutes.
50. (Previously presented) The method of claim 6, wherein said sufficient incubation time is about five minutes.
51. (Previously presented) The method of claim 4, wherein said sufficient incubation time is about ten minutes.
52. (Previously presented) The method of claim 1, wherein a level of radioincorporation of at least about 96 % is achieved.
53. (Previously presented) The method of claim 1, wherein a level of radioincorporation of at least about 97 % is achieved.
54. (Previously presented) The method of claim 1, wherein a level of radioincorporation of at least about 98 % is achieved.
55. (Previously presented) The method of claim 1, wherein a level of radioincorporation of at least about 99 % is achieved.
56. (Currently amended) The method of claim ~~5~~ 1, wherein the ~~protein or peptide~~ is an antibody fragment is selected from the group consisting of Fab, F(ab')₂, and Fv fragments.
57. (Currently amended) The method of claim ~~5~~ 4, wherein the ~~protein or peptide~~ antibody or antibody fragment is a therapeutic antibody or antibody fragment.
58. (Currently amended) The method of claim 57, wherein the ~~protein or peptide~~ antibody or antibody fragment binds specifically to CD20.
59. (Currently amended) The method of claim 57, wherein the ~~protein or peptide is~~ an antibody fragment is selected from the group consisting of Fab, F(ab')₂, and Fv fragments.
60. (Currently amended) The method of claim 1, wherein the ~~binding specificity~~ immunoreactivity is at least 50 %.

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61. (Currently amended) The method of claim 1, wherein the ~~binding specificity~~
immunoreactivity is at least 80 %.

62. (Previously presented) The method of claim 1, wherein a level of
radioincorporation greater than 96 % is achieved.

63. (Previously presented) The method of claim 1, wherein a level of
radioincorporation of from 96.3 to 99.5% is achieved.

64. (New) The method of claim 58, wherein the antibody is 2B8.

65. (New) The method of claim 64, wherein the chelator is MX-DTPA.

66. (New) The method of claim 65, wherein a level of radioincorporation
greater than 95 % is achieved.

67. (New) The method of claim 66, wherein a level of radioincorporation
greater than 96 % is achieved.

68. (New) The method of claim 67 wherein a level of radioincorporation of
from 96.3 to 99.5% is achieved.

69. (New) The method of claim 9, wherein the ratio of chelator to antibody or
antibody fragment ranges from 1½ to 1.

70. (New) The method of claim 4, wherein the specific activity of the
radiolabeled antibody or antibody fragment is over 10 mCi/mg.

71. (New) The method of claim 70, wherein the specific activity of the
radiolabeled antibody or antibody fragment is at least 15 mCi/mg.

72. (New) The method of claim 71, wherein the specific activity of the
radiolabeled antibody or antibody fragment is about 20 mCi/mg.

73. (New) The method of claim 11, wherein said acceptable temperature
ranges from about 25°C to about 43°C.

74. (New) The method of claim 12, wherein said acceptable pH is about 4.2.